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information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d stat que
L2          149 SEA FILE=REGISTRY ABB=ON  PLU=ON  AMYLOID (L) BETA (L)
                (PROTEIN OR PEPTIDE)
L3         7393 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2 OR AMYLOID (L) BETA (L)
                (PROTEIN OR PEPTIDE)
L4           42 SEA FILE=REGISTRY ABB=ON  PLU=ON  HUVEC/BI
L5         3385 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR HUVEC
L6           11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L5


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L6   ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2002:220763  HCAPLUS
DOCUMENT NUMBER:         136:243744
TITLE:                   Role of endothelin converting enzyme in catabolism of
                         amyloid .beta. peptide and
                         therapeutic and diagnostic applications
INVENTOR(S):             Eckman, Christopher B.; Eckman, Elizabeth A.
PATENT ASSIGNEE(S):      Mayo Foundation for Medical Education and Research,
                         USA
SOURCE:                  PCT Int. Appl., 40 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2002022794      A2   20020321      WO 2001-US28433  20010913
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-233012P P 20000915
US 2001-824924 A2 20010403

AB The invention describes catabolism of A.beta. by endothelin converting enzymes (ECEs). Methods of identifying compds. that upregulate ECEs are provided by the invention. Further provided by the invention are methods of regulating A.beta. catabolism in a cell and methods of decreasing the amt. of A.beta. in a cell. The invention discloses methods of diagnosing an individual with AD and methods of treating such an individual. The invention further discloses methods of identifying compds. that have anti-hypertension activity but do not cause an increase in the level of A.beta.. Further, the invention provides mutant ECE nucleic acids and mutant ECE polypeptides.

L6 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:89836 HCAPLUS
DOCUMENT NUMBER: 136:129061
TITLE: Panaxatriol compounds and their use in the treatment of conditions requiring stimulation of angiogenesis
INVENTOR(S): Sengupta, Shiladitya; Fan, Tai-Ping; Toh, Sue-Anne Ee Shiow; Wong, Ngok Shun Ricky; Yueng, Hin Wing; Leung, Hi Wun; Yue, Ying Kit Patrick; Wong, Yuk Ling Daisy
PATENT ASSIGNEE(S): Cambridge University Technical Services Limited, UK; Hong Kong Baptist University
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002007732	A2	20020131	WO 2001-GB3360	20010726

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-18388 A 20000726
GB 2001-5613 A 20010307

AB The invention provides the use of panaxatriol for the treatment of conditions requiring stimulation of angiogenesis, and the use of panaxatriol in the manuf. of medicaments for such treatment. Preferably the panaxatriol is the naturally-occurring ginsenoside Rg1.

L6 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:785622 HCAPLUS
DOCUMENT NUMBER: 135:314495

TITLE: Differentially expressed nucleic acids encoding tumor-associated proteins, kits, and methods for identification, assessment, prevention, and therapy of human prostate cancer
INVENTOR(S): Schlegel, Robert; Endege, Wilson; Monahan, John E.
PATENT ASSIGNEE(S): Millennium Predictive Medicine, Inc., USA
SOURCE: PCT Int. Appl., 975 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053836	A2	20010726	WO 2001-US2318	20010124
WO 2001053836	A3	20020606		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2000-178525P P 20000124
US 2000-183245P P 20000217
US 2000-190139P P 20000316
US 2000-208126P P 20000531
US 2000-219705P P 20000718
US 2000-255160P P 20001213

AB This invention relates to newly discovered correlations between expression of certain nucleic acid markers and the cancerous state of human prostate cells. The levels of expression of individual markers and combinations of markers described herein correlates with the presence of prostate cancer or a pre-malignant condition in a patient. Methods are provided for detecting the presence of prostate cancer in a sample, the absence of prostate cancer in a sample, the stage of a prostate cancer, the metastatic potential of a prostate cancer, the indolence or aggressiveness of the cancer, and other characteristics of prostate cancer that are relevant to prevention, diagnosis, characterization and therapy of prostate cancer in a patient. Thousands of differentially-expressed cDNA markers are identified in subtracted cDNA libraries and by transcript profiling. [This abstr. record is the fourth of four records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

IT **151002-40-3 183050-30-8**
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(nucleotide sequence; differentially expressed nucleic acids encoding tumor-assocd. proteins, kits, and methods for identification, assessment, prevention, and therapy of human prostate cancer)

L6 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:250634 HCAPLUS
DOCUMENT NUMBER: 130:295047
TITLE: Thrombin induces surface and intracellular secretion

of amyloid precursor protein from human endothelial cells
AUTHOR(S): Ciallella, John R.; Figueiredo, Helmer; Smith-Swintosky, Virginia; McGillis, Joseph P.
CORPORATE SOURCE: Department Microbiology Immunology, College Medicine, University Kentucky, Lexington, KY, USA
SOURCE: Thrombosis and Haemostasis (1999), 81(4), 630-637
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: F. K. Schattauer Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thrombin, a major coagulant and inflammatory mediator, was shown to regulate **amyloid** precursor **protein** (APP) secretion. APP is the **protein** from which the **amyloid** . **beta**. **peptide** (A.**beta**.) is derived. A. **beta**. forms the core of vascular and cerebral plaques in Alzheimer's disease (AD). Human umbilical vein endothelial cells (**HUVEC**) were used to examine the effects of thrombin on APP expression. Cell supernatants from thrombin-treated **HUVEC** were immunoblotted to measure secreted APP. Thrombin-induced secretion of APP peaks at approx. 30 min post-treatment. Immunohistochem. anal. found that APP is not colocalized with or secreted through the same pathway as coagulation factor VIII. The secretion of APP is thrombin receptor-mediated, since it is inhibited by the thrombin antagonist N-Acetyl-D-Phe-Pro1Amido-4-Guanidino-Butyl-1-Boronic acid. It also is induced by treatment with a Ca ionophore. APP secretion is **protein** kinase C (PKC)-dependent because it is blocked by the PKC inhibitor bisindolylmaleimide. APP secretion also occurs from the cell surface, possibly through direct cleavage by thrombin. Immunoreactivity on the surface of **HUVEC** decreased after thrombin treatment but not after treatment with a non-proteolytic thrombin receptor activator. These data suggest that thrombin induces APP secretion through a PKC-dependent mechanism, as well as from the cell surface. These results are consistent with thrombin playing a role in Alzheimer" disease pathol.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:714682 HCAPLUS
DOCUMENT NUMBER: 130:123280
TITLE: Brain endothelial cell enzymes cleave platelet-retained amyloid precursor protein
AUTHOR(S): Davies, Theresa A.; Billingslea, Andrea M.; Long, Heidi J.; Tibbles, Heather; Wells, John M.; Eisenhauer, Patricia B.; Smith, Sally J.; Cribbs, David H.; Fine, Richard E.; Simons, Elizabeth R.
CORPORATE SOURCE: Boston University School of Medicine, Boston, MA, USA
SOURCE: Journal of Laboratory and Clinical Medicine (1998), 132(4), 341-350
CODEN: JLCMAK; ISSN: 0022-2143
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have previously demonstrated that thrombin-activated platelets from patients with advanced Alzheimer's disease (AD) retain significantly more surface membrane-bound **amyloid** precursor **protein** (mAPP) than platelets from non-demented age-matched individuals (AM). We have studied interactions between these platelets and the cerebrovascular endothelium to which activated platelets adhere in a model system, investigation their involvement in the formation of **amyloid** .

beta. peptide (A.**beta.**) deposits in AD patients. We report here that there appear to be .alpha. and .**beta.** secretase-like activities in primary human blood brain barrier endothelial cell (BEC) cultures from both AD patients and AM control subjects (AD-BEC and AM-BEC, resp.) as well as a .gamma. secretase-like activity that appears only in AD-BEC. No such activities were obsd. in human umbilical vein endothelial cells (**HUVECs**). Furthermore, there is more penetration of the platelet-released products platelet factor 4 and sol. APP through the BEC layer grown from AD patients than that grown from AM individuals, whereas none penetrate through a **HUVEC** layer. Thus the interaction between platelets, the APP they have retained or released, and cerebral vascular endothelial cells may be at least partially responsible for amyloidogenic deposits around the cerebral vasculature of AD patients.

IT **158736-49-3**, Secretase
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(.alpha. and **.beta.** and .gamma.; human brain endothelial cells express surface **amyloid** precursor **protein** -cleaving enzymes in Alzheimer's disease in relation to **amyloid** **.beta. peptide** deposition)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:588522 HCAPLUS
DOCUMENT NUMBER: 129:285823
TITLE: The amyloid precursor protein (APP) and the angiotensin converting enzyme (ACE) secretase are inhibited by hydroxamic acid-based inhibitors
AUTHOR(S): Parvathy, S.; Hussain, Ishrut; Karran, Eric H.; Turner, Anthony J.; Hooper, Nigel M.
CORPORATE SOURCE: School of Biochemistry and Molecular Biology, University of Leeds, Leeds, LS2 9JT, UK
SOURCE: Biochemical Society Transactions (1998), 26(3), S242
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of batimastat, marimastat, and BB2116 have been directly compared in IMR-32 cells transfected with a cDNA encoding human ACE and **HUVECs** which endogenously express both APP and ACE. Batimastat, marimastat, and BB2116 at 20 .mu.M substantially inhibited the release of both sAPP.alpha. and ACE from transfected IMR-32 cells, while batimastat and BB2116 and 5 .mu.M substantially inhibited the release of the 2 proteins in **HUVECs**. A biotinylated deriv. of the hydroxamic acid-based inhibitor AMG-2380 completely inhibited .alpha.-secretase activity. Complete inhibition of .alpha.-secretase activity by the biotinylated form of the inhibitor shows that .alpha.-secretase activity is predominantly found at the cell surface.

IT **158736-49-3**, .alpha.-Secretase
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(amyloid precursor protein (APP) and angiotensin-converting enzyme (ACE) secretase are inhibited by hydroxamic acid-based inhibitors)

L6 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:56259 HCAPLUS

DOCUMENT NUMBER: 128:177497
TITLE: Alzheimer's Amyloid Precursor Protein .alpha.-Secretase Is Inhibited by Hydroxamic Acid-Based Zinc Metalloprotease Inhibitors: Similarities to the Angiotensin Converting Enzyme Secretase
AUTHOR(S): Parvathy, S.; Hussain, Ishrut; Karran, Eric H.; Turner, Anthony J.; Hooper, Nigel M.
CORPORATE SOURCE: School of Biochemistry and Molecular Biology, University of Leeds, Leeds, LS2 9JT, UK
SOURCE: Biochemistry (1998), 37(6), 1680-1685
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 4 kDa .**beta**.-**amyloid peptide** that forms the **amyloid** fibrils in the brain parenchyma of Alzheimer's disease patients is derived from the larger integral membrane **protein**, the **amyloid** precursor **protein**. In the nonamyloidogenic pathway, .alpha.-secretase cleaves the **amyloid** precursor **protein** within the .**beta**.-**amyloid** domain, releasing an extracellular portion and thereby preventing deposition of the intact amyloidogenic **peptide**. The release of the **amyloid** precursor **protein** from both SH-SY5Y and IMR-32 neuronal cells by .alpha.-secretase was blocked by batimastat and other related synthetic hydroxamic acid-based zinc metalloprotease inhibitors, but not by the structurally unrelated zinc metalloprotease inhibitors enalaprilat and phosphoramidon. Batimastat inhibited the release of the **amyloid** precursor **protein** from both cell lines with an I50 value of 3 mM. Removal of the thienothiomethyl substituent adjacent to the hydroxamic acid moiety or the substitution of the P2' substituent decreased the inhibitory potency of batimastat toward .alpha.-secretase. In the SH-SY5Y cells, both the basal and the carbachol-stimulated release of the **amyloid** precursor **protein** were blocked by batimastat. In contrast, neither the level of full-length **amyloid** precursor **protein** nor its cleavage by .**beta**.-secretase were inhibited by any of the zinc metalloprotease inhibitors examd. In transfected IMR-32 cells, the release of both the **amyloid** precursor **protein** and angiotensin converting enzyme was inhibited by batimastat, marimastat, and BB2116 with I50 values in the low micromolar range, while batimastat and BB2116 inhibited the release of both **proteins** from **HUVECs**. The profile of inhibition of .alpha.-secretase by batimastat and structurally related compds. is identical with that obsd. with the angiotensin converting enzyme secretase suggesting that the two are closely related zinc metalloproteases.

IT **158736-49-3**, .alpha.-Secretase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Alzheimer's amyloid precursor protein .alpha.-secretase is inhibited by hydroxamic acid-based zinc metalloprotease inhibitors)

L6 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:446214 HCAPLUS
DOCUMENT NUMBER: 122:211809
TITLE: Enhanced processing of APP induced by IL-1.beta. can be reduced by indomethacin and nordihydroguaiaretic acid
AUTHOR(S): Dash, Pramod K.; Moore, Anthony N.

CORPORATE SOURCE: Department of Neurobiology and Anatomy, University of Texas Health Science Center, Houston, TX, 77225, USA
SOURCE: Biochem. Biophys. Res. Commun. (1995), 208(2), 542-8
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Abnormal processing the **amyloid** precursor **protein** (APP) is though to contribute to the formation of **amyloid** plaques in Alzheimer's disease. Several studies suggest that inflammation, and possibility the cytokines released during the inflammatory process, may participate in the plaque formation. The authors have utilized a cell culture system to examine the effects of the cytokine interleukin-1.**beta**. (IL-1.**beta**.) on the processing of APP. The authors present data to show that IL-1.**beta**. increases the maturation of APP and causes enhanced processing of the full length APP isoforms. In addn., as reported previously in **HUVEC** cells, IL-1.**beta**. increases the secretion of APP in PC12 cells. Indomethacin and NDGA, reported inhibitors of the cyclooxygenase and lipoxygenase pathways, resp., block these effects, suggesting the involvement of prostaglandins and leukotrienes in IL-1.**beta**. mediated APP processing.

L6 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:267385 HCAPLUS
DOCUMENT NUMBER: 120:267385
TITLE: Heat shock alters Alzheimer's .**beta**. **amyloid** precursor **protein** expression in human endothelial cells
AUTHOR(S): Ciallella, J. R.; Rangnekar, V. V.; McGillis, J. P.
CORPORATE SOURCE: Sanders-Brown Cent. Aging, Univ. Kentucky Coll. Med., Lexington, KY, 40536-0084, USA
SOURCE: J. Neurosci. Res. (1994), 37(6), 769-76
CODEN: JNREDK; ISSN: 0360-4012
DOCUMENT TYPE: Journal
LANGUAGE: English
AB One of the pathol. lesions in Alzheimer's disease (AD) is the **amyloid** or senile plaque. The plaque core is predominantly made up of **amyloid beta peptide** (A.**beta**.), a 42-43 amino acid **peptide** derived from **amyloid** precursor **protein** (APP). APP is a membrane bound glycoprotein which is expressed ubiquitously in many cells. Although normal or pathol. functions for APP are not well understood, several observations suggest that APP may play a role in cellular stress and inflammation at the endothelial cell/vascular barrier. APP is found in platelets and endothelial cells, it can inhibit a blood coagulation factor, and secreted APP can be neuroprotective. Changes in expression of APP during cellular stress or inflammation may contribute to pathol. deposition of A.**beta**.. In the present studies, expression of APP in human endothelial cells was examd. following heat shock. In human umbilical vein endothelial cells (**HUVECs**) exposed to 42.degree.C for 30 min, there was a five- to eight-fold increase in APP mRNA levels which peaked at 4 h. The increase in APP mRNA was followed by an increase in APP **protein** immunoreactivity in the cytoplasm in a perinuclear Golgi-like region, and in discrete granular cytoplasmic structures. Immunoblot anal. of APP in the cell media found a transient increase in APP which peaked at 1 h after heat shock. These results suggest that cellular stress induces the secretion of APP from endothelial cells followed by a subsequent increase in APP mRNA and **protein** synthesis. The upregulation of APP mRNA and **protein** supports a cellular stress role for APP.

L6 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:442277 HCAPLUS
DOCUMENT NUMBER: 119:42277
TITLE: Interleukin-1-inducible genes in endothelial cells. Cloning of a new gene related to C-reactive protein and serum amyloid P component
AUTHOR(S): Breviario, Ferruccio; D'Aniello, Elisabetta M.; Golay, Josee; Peri, Giuseppe; Bottazzi, Barbara; Bairoch, Amos; Saccone, Salvatore; Marzella, Rosalia; Predazzi, Valentina; et al.
CORPORATE SOURCE: Ist. Ric. Farmacol. "Mario Negri", Milan, 20157, Italy
SOURCE: J. Biol. Chem. (1992), 267(31), 22190-7
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Differential screening of a cDNA library constructed from human umbilical vein endothelial cells exposed for 1 h to interleukin-1.**beta.** (IL-1.**beta.**) has led to the identification of a novel gene (PTX3) encoding a product related to pentaxins (C-reactive **protein** and serum **amyloid** P component in man), a subclass of acute phase **proteins**. Sequencing of the full-length cDNA clone and RNase mapping revealed that the PTX3 transcript is 1861 base pairs long and has a unique transcription start site. The predicted **protein** sequence of 381 amino acids is highly similar to pentaxins in its COOH-terminal half where it also contains a typical 8-amino acid pentaxin signature sequence. The NH2-terminal half of PTX3 shows no similarity to any known **protein** sequence and initiates with a putative signal **peptide** indicating that PTX3 is secreted. The genome of PTX3 is organized into 3 exons. Interestingly, the region of homol. between PTX3 and pentaxins corresponds to the third PTX3 exon. The PTX3 gene has been localized on human chromosome 3 band q25 by Southern blots of somatic cell hybrids and by in situ hybridization. The PTX3 mRNA is induced in endothelial, hepatic, and fibroblastic cells by IL-1.**beta.** and tumor necrosis factor .alpha. but not by IL-6 and interferon-.gamma.. PTX3 may represent a novel marker of inflammatory reactions, particularly those involving the vessel wall.
IT **147245-58-7**, GenBank X63613
RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence of)

L6 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:5817 HCAPLUS
DOCUMENT NUMBER: 112:5817
TITLE: Interleukin 1 regulates synthesis of **amyloid .beta.-protein** precursor mRNA in human endothelial cells
AUTHOR(S): Goldgaber, Dmitry; Harris, Herbert W.; Hla, Timothy; Maciag, Thomas; Donnelly, Robert J.; Jacobsen, J. Steven; Vitek, Michael P.; Gajdusek, D. Carleton
CORPORATE SOURCE: Dep. Psychiatry Behav. Sci., State Univ. New York, Stony Brook, NY, 11794-8101, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1989), 86(19), 7606-10
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The modulation of **amyloid .beta.-protein** precursor (APP) gene expression was analyzed in human umbilical vein endothelial cells (**HUVEC**). The level of the APP mRNA

transcripts increased as **HUVEC** reached confluency. In confluent culture the half-life of the APP mRNA was 4 h. Treatment of the cells with human recombinant interleukin 1 (IL-1), phorbol 12-myristate 13-acetate, or heparin-binding growth factor 1 enhanced the expression of APP gene in these cells, but Ca ionophore A23187 and dexamethasone did not. The **protein** kinase C inhibitor H7 inhibited IL-1-mediated increase of the level of APP transcripts. To map IL-1-responsive elements of the APP promoter, truncated portions of the APP promoter located between position -485 and -305 upstream from the transcription start site was necessary for IL-1-mediated induction of the reporter gene. This region contains the upstream transcription factor AP-1 binding site. Thus, IL-1 upregulates APP gene expression in **HUVEC** through a pathway mediated by **protein** kinase C, utilizing the upstream AP-1 binding site of the APP promoter.

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=> d stat que
L2          149 SEA FILE=REGISTRY ABB=ON  PLU=ON  AMYLOID (L) BETA (L)
                (PROTEIN OR PEPTIDE)
L3         7393 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2 OR AMYLOID (L) BETA (L)
                (PROTEIN OR PEPTIDE)
L4           42 SEA FILE=REGISTRY ABB=ON  PLU=ON  HUVEC/BI
L5         3385 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR HUVEC
L6           11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L5
L7          142 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 (L) ENDOTHEL?
L12         879 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND BETA (W) 1 (W)(40 OR
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L13          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 AND L7
L14          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 NOT L6
L15          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND (CULTUR? OR ASSAY? OR
                ANTIBOD? OR AB#)

=> d ibib abs hitrn l15 tot

L15  ANSWER 1 OF 15  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2001:918699  HCAPLUS
TITLE:                   Gene expression profiling of amyloid
                         beta peptide-stimulated human
                         post-mortem brain microglia
AUTHOR(S):               Walker, Douglas G.; Lue, Lih-Fen; Beach, Thomas G.
CORPORATE SOURCE:        Sun Health Research Institute, Sun City, AZ, 85351,
                         USA
SOURCE:                  Neurobiology of Aging (2001), 22(6), 957-966
                         CODEN: NEAGDO; ISSN: 0197-4580
PUBLISHER:               Elsevier Science Inc.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Activation of microglia is a central part of the chronic inflammatory
     processes in Alzheimer's disease (AD). In the brains of AD patients,
     activated microglia are assocd. with amyloid beta (A.
     beta.) peptide plaques. A no. of previous studies have
     shown that aggregated synthetic A.beta. peptide
     activates cultured microglia to produce a range inflammatory
     products. The full extent of the inflammatory response still remains to
     be detd. In this study, gene array technol. was employed to investigate
     in a more extensive manner the consequences of microglial activation by A.
     beta. peptide. RNA was prepd. from pooled samples of
     cortical human microglia isolated from post-mortem cases and incubated
     with a low dose (2.5 .mu.M) of A.beta.1-42
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(or **peptide** solvent) for 24 h. This material was used to prep. cDNA probes, which were used to detect the differential pattern of expressed genes on a 1,176 Clontech membrane gene array. Results obtained showed that 104 genes were either upregulated or downregulated by 1.67 fold or greater. The most highly induced genes belonged to the chemokine family with interleukin-8 (IL-8) expression being increased by 11.7 fold. Interestingly, many of the highly induced genes had been identified as being responsive to activation by the transcription factor NF-.kappa.B. A no. of genes were downregulated. Thymosin **beta**, prothymosin alpha and parathymosin, all belonging to the same gene family, were downregulated. To validate these semi-quant. results, the expression of intercellular adhesion mol.-1 (ICAM-1) and rhoB were measured by RT-PCR in samples of cDNA derived from A.**beta**. and control stimulated human cortical microglia. These results confirm the usefulness of the gene array approach for studying A.**beta**.-mediated inflammatory processes.

IT INDEXING IN PROGRESS

IT **107761-42-2**, Glycopeptide (human clone 9-110 **amyloid** A4 **peptide** moiety)
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(gene expression profiling of **amyloid beta peptide**-stimulated human post-mortem brain microglia)

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:716108 HCAPLUS
DOCUMENT NUMBER: 136:245685
TITLE: **Amyloid .beta. peptide**-induced cerebral **endothelial** cell death involves mitochondrial dysfunction and caspase activation
AUTHOR(S): Xu, Jan; Chen, Shawei; Ku, Grace; Ahmed, S. Hinan; Xu, Jinming; Chen, Hong; Hsu, Chung Y.
CORPORATE SOURCE: Department of Neurology and Center for the Study of Nervous System Injury, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Journal of Cerebral Blood Flow and Metabolism (2001), 21(6), 702-710
CODEN: JCBMDN; ISSN: 0271-678X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Amyloid .beta. peptide** (A.**beta**.), a 39 to 43 amino acid fragment of the .**beta**.-**amyloid** precursor **protein** (.**beta**.APP), forms insol. fibrillar accumulation in neurofibrillary tangles and vascular plaques. A. **beta**. was implicated in neuronal and vascular degeneration in brain regions susceptible to plaque formation because of its cytotoxic effect on neurons and **endothelial** cells (ECs). The authors used a murine cerebral **endothelial** cell (CEC) line and primary **cultures** of bovine CECs to explore the cytotoxic mechanism of A. **beta**.. A.**beta**. **1-40** and A. **beta**. 25-35 **peptides** caused cell death in a dose-dependent and time-dependent manner. Exposure to either A. **beta**. 25-35 or A.**beta**. **1-40** at 10 .mu.mol/L for 48 h caused at least 40% cell death. Cerebral **endothelial** cell death was characterized by nuclear condensation, mitochondrial dysfunction, and nuclear and mitochondrial DNA damage. A. **beta**. 25-35 activated both caspase-8 and caspase-3 in murine CECs.

ZVAD-fmk, a broad-spectrum caspase inhibitor, prevented A.**beta**. 25-35-induced increase in caspase-3 activity and CEC death. N-acetyl-cysteine, an antioxidant, also prevented A.**beta** .-induced cell death. Together, these findings indicate that A. **beta**.-mediated CEC death is an apoptotic process that is characterized by increased oxidative stress, caspase activation, mitochondrial dysfunction, and nuclear and mitochondrial DNA damage.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:374507 HCAPLUS
DOCUMENT NUMBER: 135:120648
TITLE: In vitro studies of **amyloid .beta** .-**protein** fibril assembly and toxicity provide clues to the aetiology of Flemish variant (Ala692 .fwdarw. Gly) Alzheimer's disease
AUTHOR(S): Walsh, Dominic M.; Hartley, Dean M.; Condron, Margaret M.; Selkoe, Dennis J.; Teplow, David B.
CORPORATE SOURCE: Center for Neurologic Diseases, Brigham and Women's Hospital, Boslon, MA, 02115, USA
SOURCE: Biochemical Journal (2001), 355(3), 869-877
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In a Flemish kindred, an Ala692 .fwdarw. Gly amino acid substitution in the **amyloid .beta.-protein** precursor (A. **beta**.PP) causes a form of early-onset Alzheimer's disease (AD) which displays prominent **amyloid** angiopathy and unusually large senile plaque cores. The mechanistic basis of this Flemish form of AD is unknown. Previous in vitro studies of **amyloid .beta.-protein** (A.**beta**.) prodn. in HEK-293 cells transfected with cDNA encoding Flemish A.**beta**.PP have shown that full-length [A.**beta**.(**1-40**)] and truncated [A. **beta**.(5-40) and A.**beta**.(11-40)] forms of A.**beta** . are produced. In an effort to det. how these **peptides** might contribute to the pathogenesis of the Flemish disease, comparative biophys. and neurotoxicity studies were performed on wild-type and Flemish A.**beta**.(**1-40**), A.**beta**.(5-40) and A.**beta**.(11-40). The results revealed that the Flemish amino acid substitution increased the soly. of each form of **peptide**, decreased the rate of formation of thioflavin-T-pos. assemblies, and increased the SDS-stability of **peptide** oligomers. Although the kinetics of **peptide** assembly were altered by the Ala21 .fwdarw. Gly substitution, all three Flemish variants formed fibrils, as did the wild-type **peptides**. Importantly, toxicity studies using **cultured** primary rat cortical cells showed that the Flemish assemblies were as potent a neurotoxin as were the wild-type assemblies. The authors' results are consistent with a pathogenetic process in which conformational changes in A.**beta**. induced by the Ala21 .fwdarw. Gly substitution would facilitate **peptide** adherence to the vascular **endothelium**, creating nidi for **amyloid** growth. Increased **peptide** soly. and assembly stability would favor formation of larger deposits and inhibit their elimination. In addn., increased concns. of neurotoxic assemblies would accelerate neuronal injury and death.

IT **131438-79-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(in vitro studies of **amyloid .beta.-protein**

fibril assembly and toxicity provide clues to etiol. of Flemish variant (Ala692 .fwdarw. Gly) Alzheimer's disease in humans)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:293273 HCAPLUS
DOCUMENT NUMBER: 135:90792
TITLE: Amyloid .**beta.**(**1-42**) and its .beta.(25-35) fragment induce in vitro phosphatidylcholine hydrolysis in bovine retina capillary pericytes
AUTHOR(S): Lupo, G.; Anfuso, C. D.; Assero, G.; Strosznajder, R. P.; Walski, M.; Pluta, R.; Alberghina, M.
CORPORATE SOURCE: Department of Biochemistry, Faculty of Medicine, Viale A. Doria 6, University of Catania, Catania, 95125, Italy
SOURCE: Neuroscience Letters (2001), 303(3), 185-188
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors describe the inhibitory effect of full-length A.**beta**.(**1-42**) and A.**beta**.(25-35) fragment of **amyloid-.beta. peptide** on phosphatidylcholine (PtdCho) metab. in bovine retina capillary pericytes. Cell **cultures** were incubated with A.**beta**.s for 24 h. Peroxidn. indexes (malondialdehyde and lactate dehydrogenase release) significantly increased after 20-50 .mu.M A.**beta**.(**1-42**) or A.**beta**.(25-35) treatment. In addn., [Me-3H]choline incorporation into PtdCho strongly decreased while either 3H-choline or 14C-arachidonic acid release from prelabeled cells increased, indicating PtdCho hydrolysis. The effect was very likely due to prooxidant action of both A.**beta**. **peptides**. Reversed-sequence A.**beta**.(35-25) **peptide** did not depress 3H-choline incorporation nor stimulate PtdCho breakdown. With addn. of A.**beta**.s at low concns. (2-20 .mu.M) to pericytes, marked ultrastructural changes, well connected to metabolic alterations, emerged including shrinkage of cell bodies, retraction of processes, disruption of the intracellular actin network. Cells treated with higher concns. (50-200 .mu.M) displayed characteristics of necrotic cell death. The data suggest that: (a) A.**beta**.(**1-42**) and A.**beta**.(25-35) **peptides** may modulate phospholipid turnover in microvessel pericytes; (b) together with **endothelial** cells, pericytes could be the target of vascular damage during processes involving **amyloid** accumulation.
IT **107761-42-2**, Glycopeptide (human clone 9-110 **amyloid** A4 **peptide** moiety) **131602-53-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**amyloid .beta.**(**1-42**) and .**beta**.(25-35) fragment induce in vitro phosphatidylcholine hydrolysis in bovine retina capillary pericytes)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:910648 HCAPLUS
DOCUMENT NUMBER: 134:176793
TITLE: .beta.-Amyloid-induced migration of monocytes across human brain endothelial cells involves RAGE and

PECAM-1

AUTHOR(S): Giri, Ranjit; Shen, Yamin; Stins, Monique; Yan, Shi Du; Schmidt, Ann Marie; Stern, David; Kim, Kwang-Sik; Zlokovic, Berislav; Kalra, Vijay K.

CORPORATE SOURCE: Departments of Biochemistry and Molecular Biology, University of Southern California Keck School of Medicine, Los Angeles, CA, 90033, USA

SOURCE: American Journal of Physiology (2000), 279(6, Pt. 1), C1772-C1781
CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In patients with **amyloid .beta.**-related cerebrovascular disorders, e.g., Alzheimer's disease, one finds increased deposition of **amyloid peptide** (A.**beta.**) and increased presence of monocyte/microglia cells in the brain. However, relatively little is known of the role of A.**beta.** in the trafficking of monocytes across the blood-brain barrier (BBB). Our studies show that interaction of A.**beta.1-40** with monolayer of human brain **endothelial** cells results in augmented adhesion and transendothelial migration of monocytic cells (THP-1 and HL-60) and peripheral blood monocytes. A.**beta.**40. The A.**beta.**-mediated migration of monocytes was inhibited by **antibody** to A.**beta.** receptor (RAGE) and platelet **endothelial** cell adhesion mol. (PECAM-1). Addnl., A.**beta** .-induced transendothelial migration of monocytes were inhibited by **protein** kinase C inhibitor and augmented by phosphatase inhibitor. We conclude that interaction of A.**beta.** with RAGE expressed on brain **endothelial** cells initiates cellular signaling leading to the transendothelial migration of monocytes. We suggest that increased diapedesis of monocytes across the BBB in response to A.**beta.** present either in the peripheral circulation or in the brain parenchyma may play a role in the pathophysiol. of A.**beta.**-related vascular disorder.

IT **131438-79-4**, Human .**beta.**-**amyloid** **peptide**(1-40)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.**beta.**-**Amyloid**-induced migration of monocytes across human brain **endothelial** cells involves RAGE and PECAM-1)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:404837 HCAPLUS

DOCUMENT NUMBER: 133:133673

TITLE: Toxicity of various **amyloid .beta.** **peptide** species in **cultured** human blood-brain barrier **endothelial** cells: increased toxicity of Dutch-type mutant

AUTHOR(S): Eisenhauer, Patricia B.; Johnson, Robin J.; Wells, John M.; Davies, Theresa A.; Fine, Richard E.

CORPORATE SOURCE: Geriatric Research Center, Bedford, MA, USA

SOURCE: Journal of Neuroscience Research (2000), 60(6), 804-810
CODEN: JNREDK; ISSN: 0360-4012

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **amyloid .beta. peptide** (A.**beta**.) is the major component of the neuritic and cerebrovascular **amyloid** plaques that are one of the characteristic features of Alzheimer's disease (AD). This **peptide** has been shown to be toxic to several relevant cell types, including neurons, cerebrovascular smooth muscle cells, and **endothelial** cells. The authors have studied the toxic effects of both sol. and aggregated species of A.**beta.1-40** and the mutation A.**beta**.1-40Glu.fwdarw.Gln22, which is the major species deposited in the cerebrovascular blood vessels of victims of hereditary cerebral hemorrhage with amyloidosis, Dutch type. The authors find that aggregates of both **peptides**, as well as of A.**beta.1-42** and A.**beta**.25-35, are toxic to **cultured** human cerebrovascular **endothelial** cells (hBEC) obtained from the brain of a victim of AD (at doses lower than those that are toxic to CNS neurons or leptomeningeal smooth muscle cells). Sol. A.**beta.1-40** Gln22 is equally toxic to hBEC, whereas wild-type A.**beta.1-40** is toxic only at higher doses. This toxicity is seen at the lowest dose of A.**beta.1-40** Gln22 used, 20 nM. The sol. A.**beta**.1-40Gln22 aggregates on the surface of the cells, in contrast to A.**beta.1-40**, and its toxicity can be blocked both by an inhibitor of free radical formation and by Congo red, which inhibits **amyloid** fibril formation. The authors discuss the possibility that the enhanced toxicity of A.**beta**.1-40Gln22 is mediated by a A.**beta**. receptor on the **endothelial** cells.

IT **107761-42-2**, Glycopeptide (human clone 9-110 **amyloid** A4 **peptide** moiety) **131438-79-4 131602-53-4 144410-00-4**, Dutch **amyloid .beta.-protein** 1-40
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of various **amyloid .beta. peptide** species in **cultured** human blood-brain barrier **endothelial** cells and increased toxicity of Dutch-type mutant)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:704424 HCAPLUS
DOCUMENT NUMBER: 132:34199
TITLE: Amyloid .**beta**.-(**1-40**) stimulates cyclic GMP production via release of kinins in primary **cultured** endothelial cells
AUTHOR(S): Wirth, K. J.; Fink, E.; Rudolphi, K.; Heitsch, H.; Deutschlander, N.; Wiemer, G.
CORPORATE SOURCE: Industriepark Hochst, H 813, DG Cardiovascular Diseases, Hoechst Marion Roussel Deutschland, Frankfurt am Main, D-65926, Germany
SOURCE: European Journal of Pharmacology (1999), 382(1), 27-33
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Increased .beta.-amyloid prodn. is believed to play a central role in the pathogenesis of Alzheimer's disease. Amyloid is deposited not only in the brain of Alzheimer patients as senile plaques but also in the cerebral vessel wall leading to cerebral amyloid angiopathy. Freshly solubilized amyloid .**beta**.-(**1-40**) was previously reported to exert a vasoconstrictor effect. We investigated whether

amyloid .**beta**.-(**1-40**) affects the nitric oxide (NO)/cyclic GMP pathway in primary **cultured** endothelial cells from bovine aorta and rat coronary microvessels. Surprisingly, a significant increase in cyclic GMP prodn. after incubation with freshly dissolved amyloid .**beta**.-(**1-40**) was found. The stimulation of cyclic GMP prodn. could be inhibited by the bradykinin B2 receptor antagonist icatibant, the NO synthase inhibitor N-.omega.-nitro-L-arginine, the serine protease inhibitor 3,4-dichloroisocoumarin and the selective plasma kallikrein inhibitor Pefabloc PK, suggesting activation of the plasma kallikrein-kinin system. This is supported by a three- to four-fold increase in kinins in the supernatant of both types of endothelial cells after incubation with amyloid .**beta**.-(**1-40**) at concns. of 10-7 and 10-6 mol/L.

IT **131438-79-4**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(kinins role in amyloid .**beta**.-(**1-40**) stimulation of cyclic GMP formation in aortic and microvascular coronary **endothelial** cells in relation to cerebral amyloid angiopathy)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:686142 HCAPLUS
DOCUMENT NUMBER: 132:221288
TITLE: Induction of CD40 on human **endothelial** cells by Alzheimer's .**beta**.-**amyloid peptides**
AUTHOR(S): Tan, J.; Town, T.; Suo, Z.; Wu, Y.; Song, S.; Kundtz, A.; Kroeger, J.; Humphrey, J.; Crawford, F.; Mullan, M.
CORPORATE SOURCE: Roskamp Institute, University of South Florida, Tampa, FL, USA
SOURCE: Brain Research Bulletin (1999), 50(2), 143-148
CODEN: BRBUDU; ISSN: 0361-9230
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Growing evidence suggests that .**beta**.-**amyloid** (A.**beta**.) **peptides** play a central role in mediating vascular **endothelium** dysfunction, but the extent to which immune mechanisms are involved in this process remains unclear. To explore such mechanisms, we incubated **cultured** human aortic **endothelial** cells (HAEC) with freshly solubilized A.**beta**. and examd. expression of a central immunoregulatory mol., CD40, in these cells using reverse transcriptase-polymerase chain reaction, Western immunoblotting, and Flow cytometry. Treatment of **endothelial** cells with A.**beta**.**1-40**, A.**beta**.**1-42** or gamma interferon (IFN-.gamma.) results in a dose-dependent induction of **endothelial** CD40 expression. Furthermore, ligation of **endothelial** CD40 and simultaneous treatment of human **endothelial** cells with IFN-.gamma. or A.**beta**. **peptides** leads to a significant release of interleukin-1.**beta**. (IL-1.**beta**.), a marker for **endothelial** cell activation. Since IL-1.**beta**. is an important inflammatory response mediator, these findings suggest that the functional role of A.**beta**.-induced **endothelial** CD40

may be promotion of the inflammatory cascade in vascular **endothelial** cells.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:566904 HCAPLUS
DOCUMENT NUMBER: 129:314447

TITLE: Amyloid-.beta. induces chemokine secretion and monocyte migration across a human blood-brain barrier model

AUTHOR(S): Fiala, Milan; Zhang, Ling; Gan, Xiaohu; Sherry, Barbara; Taub, Dennis; Graves, Michael C.; Hama, Suzan; Way, Dennis; Weinand, Martin; Witte, Marlys; Lorton, Diane; Kuo, Yu-Min; Roher, Alex E.
CORPORATE SOURCE: Department of Medicine, UCLA School of Medicine, Los Angeles, CA, 90095-1769, USA

SOURCE: Molecular Medicine (New York) (1998), 4(7), 480-489
CODEN: MOMEF3; ISSN: 1076-1551
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aside from numerous parenchymal and vascular deposits of **amyloid .beta.** (A.**beta.**) **peptide**, neurofibrillary tangles, and neuronal and synaptic loss, the neuropathol. of Alzheimer's disease is accompanied by a subtle and chronic inflammatory reaction that manifests itself as microglial activation. However, in Alzheimer's disease, alterations in the permeability of the blood-brain barrier and chemotaxis, in part mediated by chemokines and cytokines, may permit the recruitment and transendothelial passage of peripheral cells into the brain parenchyma. Human monocytes from different donors were tested for their capacity to differentiate into macrophages and their ability to secrete cytokines and chemokines in the presence of A.**beta. 1-42**. A paradigm of the blood-brain barrier was constructed utilizing human brain **endothelial** and astroglial cells with the anatomical and physiol. characteristics obsd. in vivo. This model was used to test the ability of monocytes/macrophages to transmigrate when challenged by A.**beta. 1-42** on the brain side of the blood-brain barrier model. In **cultures** of peripheral monocytes, A.**beta. 1-42** induced the secretion of proinflammatory cytokines TNF-.alpha., IL-6, IL-1.**beta.**, and IL-12, as well as CC chemokines MCP-1, MIP-1.alpha., and MIP-1.**beta.**, and CXC chemokine IL-8 in a dose-related fashion. In the blood-brain barrier model, A.**beta. 1-42** and monocytes on the brain side potentiated monocyte transmigration from the blood side to the brain side. A.**beta. 1-42** stimulated differentiation of monocytes into adherent macrophages in a dose-related fashion. The magnitude of these proinflammatory effects of A.**beta. 1-42** varied dramatically with monocytes from different donors. In some individuals, circulating monocytes/macrophages, when recruited by chemokines produced by activated microglia and macrophages, could add to the inflammatory destruction of the brain in Alzheimer's disease.

IT **107761-42-2**, Glycopeptide (human clone 9-110 **amyloid** A4 **peptide** moiety)
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**amyloid-.beta.** induces chemokine secretion and monocyte migration across a human blood-brain barrier model and

relationship to Alzheimer's disease)

L15 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:556756 HCAPLUS
DOCUMENT NUMBER: 129:301106
TITLE: Role of peroxynitrite in the vasoactive and cytotoxic effects of Alzheimer's .beta.-amyloid1-40 peptide
AUTHOR(S): Paris, Daniel; Parker, Timothy A.; Town, Terrence; Suo, Zhiming; Fang, Chunhong; Humphrey, James; Crawford, Fiona; Mullan, Michael
CORPORATE SOURCE: Roskamp Lab., Dep. Psychiatry, Univ. South Florida, Tampa, FL, 33613, USA
SOURCE: Experimental Neurology (1998), 152(1), 116-122
CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Increasing evidence implicates oxidative stress as partially responsible for the neurodegenerative process of Alzheimer's disease (AD). Recent reports show an increased prodn. of nitrotyrosine in AD brains, suggesting that peroxynitrite is produced in excess in this disease. Furthermore, incidence of cerebral **amyloid** angiopathy in AD cases is very frequent (83%), strongly suggesting a vascular component of AD pathogenesis. We have evaluated the hypothesis that peroxynitrite could be responsible for mediating the cytotoxicity and vasoactivity induced by the **amyloid-.beta.1-40** (A. **beta.**) **peptide**. Rat brain **endothelial** cells (RBE-4) appear to be sensitive to A.**beta.**-induced toxicity but not to the cytotoxicity induced by peroxynitrite. Addn. of Cu/Zn superoxide dismutase to cell **culture** media, which is only able to clear extracellular superoxide, was not effective in blocking A. **beta.**-induced toxicity. However, we were able to partially block A.**beta.**-induced cytotoxicity by using Mn(III)tetrakis(4-benzoic acid) porphyrin (MnTBAP) which dismutes superoxide intracellularly. Yet, MnTBAP was not able to prevent the vasoactivity triggered by A. **beta.**. Moreover, addn. of peroxynitrite to rat aortae did not modulate the vasotension induced by A.**beta.**. We conclude that intracellular superoxide radicals may contribute to A.**beta** .-induced cytotoxicity. Our results also indicate that peroxynitrite does not significantly contribute to A.**beta.**-induced cytotoxicity in rat brain **endothelial** cells (RBE-4) or vasoactivity in rat aortae. These results suggest that therapeutic efforts aimed at removal of reactive oxygen species with SOD is unlikely to be beneficial for treatment of A.**beta.**-induced **endothelial** dysfunction. However, compds. that clear free radicals intracellularly may well be beneficial. (c) 1998 Academic Press.
IT **131438-79-4**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(peroxynitrite role in vasoactive and cytotoxic effects of Alzheimer's .beta.-amyloid1-40 peptide)

L15 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:552894 HCAPLUS
DOCUMENT NUMBER: 129:258891
TITLE: Human blood-brain barrier receptors for Alzheimer's amyloid-.**beta.** 1-40: asymmetrical binding, endocytosis, and transcytosis at the apical side of brain microvascular endothelial

cell monolayer

AUTHOR(S): Mackic, Jasmina B.; Stins, Monique; McComb, J. Gordon; Calero, Miguel; Ghiso, Jorge; Kim, Kwang Sik; Yan, Shi Du; Stern, David; Schmidt, Ann Marie; Frangione, Bias; Zlokovic, Berislav V.

CORPORATE SOURCE: Department of Neurological Surgery, USC School of Medicine, Los Angeles, CA, 90033, USA

SOURCE: Journal of Clinical Investigation (1998), 102(4), 734-743
CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A sol. monomeric form of Alzheimer's **amyloid**-.**beta**. (**1-40**) **peptide** (sA.**beta**.**1-40**) is present in the circulation and could contribute to neurotoxicity if it crosses the brain capillary **endothelium**, which comprises the blood-brain barrier (BBB) in vivo. This study characterizes **endothelial** binding and transcytosis of a synthetic **peptide** homologous to human sA.**beta**.**1-40** using an in vitro model of human BBB. 125I-sA.**beta**.**1-40** binding to the brain microvascular **endothelial** cell monolayer was time dependent, polarized to the apical side, and saturable with high- and low-affinity dissocn. consts. of 7.8.+-.1.2 and 52.8.+-.6.2 nM, resp. Binding of 125I-sA.**beta**.**1-40** was inhibited by anti-RAGE (receptor for advanced glycation end products) **antibody** (63%) and by acetylated low d. lipoproteins (33%). Consistent with these data, transfected **cultured** cells overexpressing RAGE or macrophage scavenger receptor (SR), type A, displayed binding and internalization of 125I-sA.**beta**.**1-40**. The internalized **peptide** remains intact >94%. Transcytosis of 125I-sA.**beta**.**1-40** was time and temp. dependent, asym. from the apical to basolateral side, saturable with a Michaelis const. of 45.+-.9 nM, and partially sensitive to RAGE blockade (36%) but not to SR blockade. We conclude that RAGE and SR mediate binding of sA.**beta**.**1-40** at the apical side of human BBB, and that RAGE is also involved in sA.**beta**.**1-40** transcytosis.

L15 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:698635 HCAPLUS

DOCUMENT NUMBER: 127:344891

TITLE: The vasoactivity of A.beta. peptides

AUTHOR(S): Crawford, Fiona; Suo, Zhiming; Fang, Chunhong; Sawar, Asad; Su, George; Arendash, Gary; Mullan, Mike

CORPORATE SOURCE: Department of Psychiatry, Roskamp Laboratories, University of South Florida, Tampa, FL, 33613, USA

SOURCE: Annals of the New York Academy of Sciences (1997), 826(Cerebrovascular Pathology in Alzheimer's Disease), 35-46
CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: New York Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have demonstrated that freshly solubilized **amyloid** A.**beta**. **peptides** can enhance vasoconstriction by phenylephrine or **endothelin** of isolated rat aorta. Concns. of **peptide** producing these effects (100 nM-1 .mu.M) are much lower than those requiring toxicity to **endothelial** cells in **culture**, and effects are immediate, not requiring the prolonged

time periods for aggregation necessary in A.**beta**. cell **culture** toxicity expts. Pretreatment with superoxide dismutase diminishes the enhancement of vasoconstriction by A.**beta**. **peptides**, suggesting that the effects are partly mediated via a decrease in the nitric oxide/superoxide ratio. Enhancement of **endothelin** vasoconstriction is obsd. with A.**beta**. **1-40** and A.**beta**.**1-42**, but not with A.**beta**.25-35 even at 5 .mu.M, again suggesting the mechanism of A.**beta**. vasoactivity is distinct from that of A. **beta**. cytotoxicity. These observations raise the possibility that A.**beta**. **peptides** in contact with the cerebrovasculature could result in vasoconstriction, hypoperfusion and oxygen free radical imbalance contributing to the neurodegeneration of Alzheimer's disease.

L15 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:420084 HCAPLUS
DOCUMENT NUMBER: 127:77065
TITLE: Superoxide free radical and intracellular calcium mediate A.**beta**.**1-42** induced endothelial toxicity
AUTHOR(S): Suo, Zhiming; Fang, Chunhong; Crawford, Fiona; Mullan, Mike
CORPORATE SOURCE: Roskamp Laboratories, Department of Psychiatry, 3515 E. Fletcher Ave., University of South Florida, Tampa, USA
SOURCE: Brain Research (1997), 762(1,2), 144-152
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To investigate the role of **amyloid** .**beta**.-**peptide** (A.**beta**.) toxicity on **endothelial** cells, we have applied **amyloid peptide** (A) **peptides** to **cultures** of human aortic **endothelial** cells (HAEC). Our results show that both A.**beta**.**1-42** and A.**beta**.25-35 are toxic to HAEC in a time- and dose-dependent manner, and that this toxicity can be partially prevented by the calcium channel blocker, verapamil, and the antioxidant, superoxide dismutase. The common form of A.**beta**., A.**beta**. **1-40**, which has been shown to be neurotoxic, is much less toxic to HAEC. A.**beta**. toxicity to HAEC occurs within 30 min of treatment with relatively lower doses than those usually obsd. in primary **cultured** neurons and vascular smooth muscle cells. It was recently reported that a variety of mutations in the .**beta**.-**amyloid protein** precursor gene and the Presenilin-1 and -2 genes linked to early-onset familial Alzheimer's disease (AD) cause an increase in the plasma concn. of A.**beta**.**1-42** in mutation carriers [Scheuner et al., Secreted **amyloid** . **beta**.-**protein** similar to that in the senile plaques of Alzheimer's disease is increased in vitro by the presenilin 1 and 2 and APP mutations linked to familial Alzheimer's disease, Nature Med., 2 (1996) 864-870]. Human aortic **endothelial** cells are more sensitive to A.**beta**.**1-42** than A.**beta** .**1-40**, via a pathway involving an excess of superoxide free radicals and influx of extracellular calcium. Finally, we have evidence that both apoptotic and necrotic processes are activated by the A.**beta**. **peptides** in these **endothelial** cells.

L15 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:286921 HCAPLUS
DOCUMENT NUMBER: 125:7354
TITLE: Glycoprotein 330/megalin: Probable role in receptor-mediated transport of apolipoprotein J alone and in a complex with Alzheimer disease amyloid .beta. at the blood-brain and blood-cerebrospinal fluid barriers
AUTHOR(S): Zlokovic, Berislav V.; Martel, Cynthia L.; Matsubara, Etsuro; McComb, J. Gordon; Zheng, Gang; McCluskey, Robert T.; Frangione, Blas; Ghiso, Jorge
CORPORATE SOURCE: Dep. Neurological Surgery, Univ. Southern California Sch. Med., Los Angeles, CA, 90033, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1996), 93(9), 4229-4234
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A sol. form of Alzheimer disease **amyloid .beta.-protein** (sA.**beta.**) is transported in the blood and cerebrospinal fluid mainly complexed with apolipoprotein J (apoJ). Using a well-characterized in situ perfused guinea pig brain model, the authors recently obtained preliminary evidence that apoJ facilitates transport of sA.**beta.1-40**-apoJ complexes across the blood-brain barrier and the blood-cerebrospinal fluid barrier, but the mechanism remain poorly understood. In the present study, the authors examd. the transport process in greater detail and investigated the possible role of glycoprotein 330 (gp330)/megalin, a receptor for multiple ligands, including apoJ. High-affinity transport systems with a Km of 0.2 and 0.5 nM were demonstrated for apoJ at the blood-brain barrier and the choroid epithelium in vivo, suggesting a specific receptor-mediated mechanism. The sA.**beta.1-40**-apoJ complex shared the same transport mechanism and exhibited 2.4- to 10.2-fold higher affinity than apoJ itself. Binding to microvessels, transport into brain parenchyma, and choroidal uptake of both apoJ and sA.**beta**.13-40-apoJ complexes were markedly inhibited (74-99%) in the presence of a monoclonal **antibody** to gp330/megalin and were virtually abolished by perfusion with the receptor-assocd. **protein**, which blocks binding of all known ligands to gp330. Western blot anal. of cerebral microvessels with the monoclonal **antibody** to gp330 revealed a **protein** with a mass identical to that in exts. to kidney membranes enriched with gp330/megalin, but in much lower concn. The findings suggest that gp330/megalin mediates cellular uptake and transport of apoJ and sA.**beta.1-40**-apoJ complex at the cerebral vascular **endothelium** and choroid epithelium.

IT **131438-79-4**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(glycoprotein 330/megalin in mediation of cellular uptake and transport of apolipoprotein J and sol. **amyloid .beta. protein**-apolipoprotein J complex at blood-brain barrier and blood-cerebrospinal fluid barrier)

L15 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:892627 HCAPLUS
DOCUMENT NUMBER: 124:4104
TITLE: Vector-mediated delivery of 125I-labeled .**beta**.-**amyloid peptide** A.**beta**.**1-40** through the blood-brain barrier and binding to Alzheimer disease **amyloid** of the A.**beta**.1-

40/vector complex

AUTHOR(S): Saito, Yasunari; Buciak, Jody; Yang, Jing; Pardridge, William M.
CORPORATE SOURCE: Sch. Med., Univ. California, Los Angeles, CA, 90024, USA

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1995), 92(22), 10227-31
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The brain **amyloid** of Alzheimer disease (AD) may potentially be imaged in patients with AD by using neuroimaging technol. and a radiolabeled form of the 40-residue .**beta.-amyloid peptide** A.**beta.1-40** that is enabled to undergo transport through the brain capillary **endothelial** wall, which makes up the blood-brain barrier (BBB) in vivo. Transport of 125I-labeled A.**beta.1-40** (125I-A.**beta.1-40**) through the BBB was found to be negligible by expts. with both an i.v. injection technique and an internal carotid artery perfusion method in anesthetized rats. In addn., 125I-A.**beta.1-40** was rapidly metabolized after either i.v. injection or internal carotid artery perfusion. BBB transport was increased and peripheral metab. was decreased by conjugation of monobiotinylated 125I-A.**beta.1-40** to a vector-mediated drug delivery system, which consisted of a conjugate of streptavidin (SA) and the OX26 monoclonal **antibody** to the rat transferrin receptor, which undergoes receptor-mediated transcytosis through the BBB. The brain uptake, expressed as percent of injected dose delivered per g of brain, of the 125I,bio-A.**beta.1-40**/SA-OX26 conjugate was 0.15 .+-. 0.01, a level that is 2-fold greater than the brain uptake of morphine. The binding of the 125I,bio-A.**beta.1-40**/SA-OX26 conjugate to the **amyloid** of AD brain was demonstrated by both film and emulsion autoradiog. performed on frozen sections of AD brain. Binding of the 125I,bio-A.**beta.1-40**/SA-OX26 conjugate to the **amyloid** of AD brain was completely inhibited by high concns. of unlabeled A.**beta.1-40**. In conclusion, these studies show that BBB transport and access to **amyloid** within brain may be achieved by conjugation of A.**beta.1-40** to a vector-mediated BBB drug delivery system.

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E1 THROUGH E4 ASSIGNED

=> sel hit rn 16
E5 THROUGH E8 ASSIGNED

=> file reg
FILE 'REGISTRY' ENTERED AT 15:34:25 ON 10 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES:    9 JUL 2002  HIGHEST RN 437979-76-5
DICTIONARY FILE UPDATES:   9 JUL 2002  HIGHEST RN 437979-76-5

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
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conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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             1 144410-00-4/BI
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             1 147245-58-7/BI
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             1 151002-40-3/BI
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               183050-30-8/BI)

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L16  ANSWER 1 OF 8  REGISTRY  COPYRIGHT 2002 ACS
RN   183050-30-8  REGISTRY
CN   DNA (human HUVEC cell mitochondria inner membrane-associated
     preprotein-transporting protein gene TIM17 subunit cDNA plus flanks) (9CI)
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Deoxyribonucleic acid (human mitochondria-associated outer membrane
     preprotein-transporting protein subunit Tim17 gene plus 5'- and
     3'-flanking region fragment)
OTHER NAMES:
CN   881: PN: WO0153836 TABLE: 3-5 claimed DNA
CN   DNA (human cell line HUVEC cDNA)
CN   DNA (human HUVEC cell mitochondria inner membrane-associated preprotein
     translocase gene TIM17 subunit cDNA plus flanks)
CN   DNA (human mitochondria-associated outer membrane preprotein-transporting
     protein subunit Tim17 gene plus flanks)
FS   NUCLEIC ACID SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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               4 REFERENCES IN FILE CA (1967 TO DATE)
               4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  135:314495
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REFERENCE 2: 134:15898

REFERENCE 3: 131:182691

REFERENCE 4: 125:295785

L16 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **158736-49-3** REGISTRY
CN .beta.-Secretase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .beta. Protein amyloidogenase
CN .beta.-Amyloid protein precursor secretase
CN .beta.-Site APP-cleaving enzyme
CN .beta.-site APP-cleaving enzyme 1
CN .beta.-site APP-cleaving enzyme 2
CN Amyloid precursor protein secretase
CN APP secretase
CN Aspartic protease BACE
CN Aspartic protease BACE1
CN Aspartic protease BACE2
CN D-Aspartyl-.beta.-amyloid secretase
CN Memapsin 1
CN Memapsin 2
CN Protease Asp1
CN Protease Asp2
CN Proteinase BACE1
CN Proteinase BACE2
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CIN, PROMT, TOXCENTER, USPATFULL

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426 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
429 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:18699

REFERENCE 2: 137:4400

REFERENCE 3: 136:401651

REFERENCE 4: 136:399874

REFERENCE 5: 136:399872

REFERENCE 6: 136:382183

REFERENCE 7: 136:367771

REFERENCE 8: 136:354491

REFERENCE 9: 136:353665

REFERENCE 10: 136:353271

L16 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2002 ACS

RN **151002-40-3** REGISTRY
CN DNA (human .beta.-amyloid precursor protein cDNA plus flanks) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO0002911 FIGURE: 1 claimed DNA
CN 1: PN: WO0153836 TABLE: 3-5 claimed DNA
CN DNA (human clone WO0118542_SEQID_6302 ovary tumor-associated protein cDNA plus flanks)
CN PN: WO0118542 SEQID: 6302 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

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4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:314495

REFERENCE 2: 135:72211

REFERENCE 3: 134:350281

REFERENCE 4: 132:102848

L16 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **147245-58-7** REGISTRY
CN DNA, (human clone PTX3/E gene PTX3 interleukin 1-inducible protein cDNA plus flanks) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid, (human clone PTX3/E gene PTX3 interleukin 1-inducible protein messenger RNA-complementary plus 5'- and 3'-flanking region fragment)
OTHER NAMES:
CN DNA (human HUVEC cell clone PTX3/E gene PTX3 cDNA plus flanks)
CN GenBank X63613
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, USPATFULL

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*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:146104

REFERENCE 2: 119:42277

L16 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **144410-00-4** REGISTRY
CN L-Valine, L-.alpha.-aspartyl-L-alanyl-L-.alpha.-glutamyl-L-phenylalanyl-L-arginyl-L-histidyl-L-.alpha.-aspartyl-L-serylglycyl-L-tyrosyl-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl-L-alanyl-L-glutaminyl-L-.alpha.-

aspartyl-L-valylglycyl-L-seryl-L-asparaginyl-L-lysylglycyl-L-alanyl-L-isoleucyl-L-isoleucylglycyl-L-leucyl-L-methionyl-L-valylglycylglycyl-L-valyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Dutch amyloid .beta.-protein 1-40
FS PROTEIN SEQUENCE
MF C194 H296 N54 O57 S
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
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24 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:4156

REFERENCE 2: 134:188228

REFERENCE 3: 134:145702

REFERENCE 4: 134:114197

REFERENCE 5: 133:320545

REFERENCE 6: 133:206277

REFERENCE 7: 133:133673

REFERENCE 8: 133:87762

REFERENCE 9: 133:57058

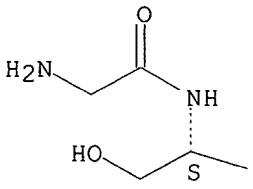
REFERENCE 10: 133:29262

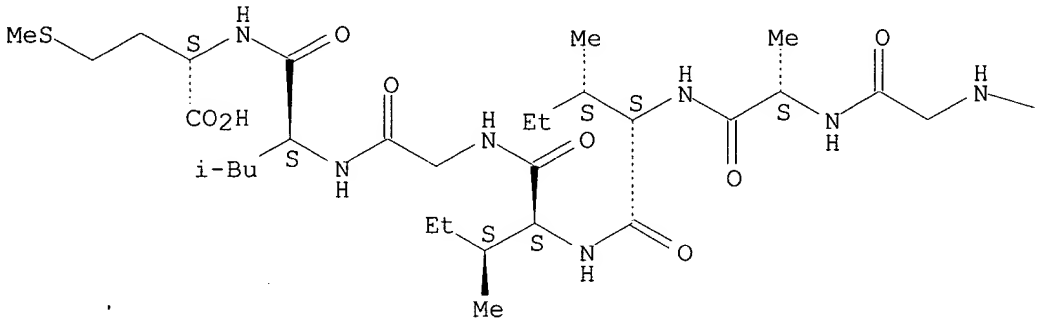
L16 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **131602-53-4** REGISTRY
CN L-Methionine, glycyl-L-seryl-L-asparaginyl-L-lysylglycyl-L-alanyl-L-isoleucyl-L-isoleucylglycyl-L-leucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Methionine, N-[N-[N-[N-[N-[N-[N-[N2-[N2-(N-glycyl-L-seryl)-L-asparaginyl]-L-lysyl]glycyl]-L-alanyl]-L-isoleucyl]-L-isoleucyl]glycyl]-L-leucyl]-
OTHER NAMES:
CN .beta.-Amyloid fragment(25-35)
CN .beta.-Amyloid peptide(25-35)
CN 1: PN: US6172043 SEQID: 10 unclaimed sequence
CN 271: PN: WO0069900 SEQID: 951 unclaimed protein
CN 304: PN: WO0069900 SEQID: 984 unclaimed protein
CN 44: PN: US6168776 PAGE: 27 claimed protein
CN 5: PN: US6043283 FIGURE: 17 claimed protein
CN Eledoisin, 1-glycine-2-L-serine-3-L-asparagine-5-glycine-7-L-isoleucine-11-L-methionine-
CN Human .beta.-amyloid peptide(25-35)
CN PN: WO9954485 SEQID: 4 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C45 H81 N13 O14 S
SR CA
LC STN Files: AGRICOLA, BIOSIS, CA, CAPLUS, CHEMCATS, CSCHEM, TOXCENTER,

USPAT2, USPATFULL

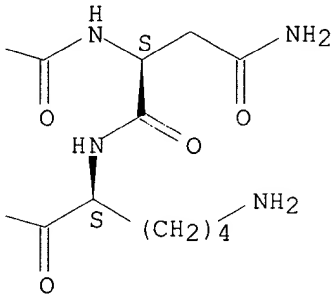
Absolute stereochemistry.

PAGE 1-A





PAGE 1-B



355 REFERENCES IN FILE CA (1967 TO DATE)
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REFERENCE 2: 136:396235

REFERENCE 3: 136:384210

REFERENCE 4: 136:367772

REFERENCE 5: 136:353658

REFERENCE 6: 136:338805

REFERENCE 7: 136:319284

REFERENCE 8: 136:319270

REFERENCE 9: 136:261625

REFERENCE 10: 136:252359

L16 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **131438-79-4** REGISTRY
CN L-Valine, L-.alpha.-aspartyl-L-alanyl-L-.alpha.-glutamyl-L-phenylalanyl-L-arginyl-L-histidyl-L-.alpha.-aspartyl-L-serylglycyl-L-tyrosyl-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-valylglycyl-L-seryl-L-asparaginyl-L-lysylglycyl-L-alanyl-L-isoleucyl-L-isoleucylglycyl-L-leucyl-L-methionyl-L-valylglycylglycyl-L-valyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .beta.-Amyloid peptide(1-40)
CN .beta.-Amyloid protein(1-40)
CN 1: PN: JP2001247600 SEQID: 1 unclaimed protein
CN 1: PN: WO0152890 SEQID: 1 claimed protein
CN 276: PN: WO0069900 SEQID: 956 unclaimed protein
CN 2: PN: WO0142306 SEQID: 2 unclaimed protein
CN 54: PN: WO0038706 SEQID: 14 unclaimed protein
CN 7: PN: US6043283 FIGURE: 17 claimed protein
CN Amyloid .beta. peptide(1-40) (synthetic)
CN Human .beta.-amyloid peptide-(1-40)
FS PROTEIN SEQUENCE
DR 149531-25-9, 257942-44-2, 281660-52-4, 292605-71-1
MF C194 H295 N53 O58 S
CI MAN
SR CA
LC STN Files: ANABSTR, BIOSIS, CA, CAPLUS, CHEMCATS, CSCHEM, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
765 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:4739

REFERENCE 2: 137:4410

REFERENCE 3: 136:400139

REFERENCE 4: 136:399865

REFERENCE 5: 136:395932

REFERENCE 6: 136:384232

REFERENCE 7: 136:384210

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REFERENCE 9: 136:367771

REFERENCE 10: 136:367769

L16 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **107761-42-2** REGISTRY
CN Glycopeptide (human clone 9-110 amyloid A4 peptide moiety) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 181: PN: WO0185208 SEQID: 174 unclaimed protein
CN 1: PN: WO0068263 FIGURE: 1 claimed protein
CN 1: PN: WO0069456 SEQID: 10 unclaimed protein
CN 1: PN: WO0182967 SEQID: 2 unclaimed protein
CN 21: PN: WO0142306 SEQID: 3 unclaimed protein
CN 275: PN: WO0069900 SEQID: 955 unclaimed protein
CN 2: PN: JP2001247600 SEQID: 2 unclaimed protein
CN 2: PN: WO0152890 SEQID: 2 claimed protein
CN 34: PN: WO0072876 PAGE: 24 unclaimed protein
CN 52: PN: WO0038706 SEQID: 10 unclaimed protein
CN 5: PN: WO0132694 SEQID: 5 claimed protein
CN 6: PN: US6043283 FIGURE: 17 claimed protein
CN 97: PN: WO0109309 PAGE: 23 unclaimed protein
CN Amyloid .beta. 1-42
CN Glycoprotein, amyloid A4 (human clone .lambda.APCP168i4 N-terminal 42-amino-acid fragment)
CN Human .beta.-amyloid peptide-(1-42)
CN L-Alanine, L-.alpha.-aspartyl-L-alanyl-L-.alpha.-glutamyl-L-phenylalanyl-L-arginyl-L-histidyl-L-.alpha.-aspartyl-L-serylglycyl-L-tyrosyl-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-valylglycyl-L-seryl-L-asparaginyl-L-lysylglycyl-L-alanyl-L-isoleucyl-L-isoleucylglycyl-L-leucyl-L-methionyl-L-valylglycylglycyl-L-valyl-L-valyl-L-isoleucyl-
CN Peptide .beta. (human amyloid)
FS PROTEIN SEQUENCE
DR 136250-78-7, 143044-07-9, 281660-50-2
MF C203 H311 N55 O60 S
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CHEMCATS, CSCHEM, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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687 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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REFERENCE 2: 137:18672

REFERENCE 3: 137:17435

REFERENCE 4: 137:4739

REFERENCE 5: 136:400445

REFERENCE 6: 136:400256

REFERENCE 7: 136:400139

REFERENCE 8: 136:399865

REFERENCE 9: 136:384964

REFERENCE 10: 136:384232